

CLAIMS

1. A method of monitoring a reduction in tumor size in a patient, comprising administering to a patient having a tumor a replication-competent Paramyxoviridae virus comprising a nucleic acid sequence encoding a heterologous polypeptide, wherein upon the administration the heterologous polypeptide is detectable in a biological fluid of said patient, and detection of said heterologous polypeptide is indicative of Paramyxoviridae virus growth in said patient and reduction in tumor size.
2. The method of claim 1 wherein said heterologous polypeptide is biologically inactive in said patient.
3. The method of claim 1 wherein said Paramyxoviridae virus comprises a chimeric gene encoding a recombinant fusion protein comprising said heterologous polypeptide fused to an endogenous polypeptide.
4. The method of claim 4 wherein said recombinant fusion protein comprises an amino acid linker sequence between said heterologous polypeptide and said endogenous polypeptide, wherein said amino acid linker sequence comprises a protease cleavage site.
5. A method of increasing the fusogenicity on tumor cells of a Paramyxoviridae virus, comprising contacting tumor cells with a replication-competent Paramyxoviridae virus comprising one or more of a recombinant F protein, H protein, or M protein of said Paramyxoviridae virus that increases fusogenicity of said virus with said cells.
6. A method of reducing tumor size in a patient, comprising administering to a patient having a tumor a replication-competent Paramyxoviridae virus comprising one or more of a recombinant F, H, or M protein of said Paramyxoviridae virus having increased fusogenicity of said virus with cells of said tumor.

7. A method of reducing tumor size in a patient, comprising administering to a patient having a tumor a replication-competent Paramyxoviridae comprising a nucleic acid sequence encoding a cytokine wherein said administration results in reduced tumor size.

8. The method of claim 7 wherein said cytokine is selected from the group consisting of : IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-12, GM-CSF, IFN- γ , and TNF- β .

9. A method of reducing tumor size in a patient, comprising administering to a patient having a tumor a Paramyxoviridae virus that is specific for cells of said tumor.

10. The method of claim 9 wherein said Paramyxoviridae virus comprises a viral surface ligand that specifically binds to a receptor on a tumor cell.

11. The method of claim 10 wherein said ligand is fused via an intervening amino acid linker to a Paramyxoviridae virus surface protein to form a ligand/virus recombinant protein such that said fusion protein specifically binds to said receptor on said tumor cell.

12. The method of claim 11 wherein said amino acid linker of said fusion protein comprises a protease cleavage site for a protease produced by said tumor cell, such that cleavage of said cleavage site by said protease produced by said tumor cell permits infection of said tumor cell by said Paramyxoviridae virus.

13. The method of claim 12 wherein said virus surface protein is one of F protein or H protein.

14. The method of claim 10 wherein said ligand is a single chain antibody specific for carcinoembryonic antigen and said tumor cell receptor is carcinoembryonic antigen.

15. The method of claim 9 wherein the furin cleavage sequence of said Paramyxoviridae virus F protein is removed and replaced with a cleavage sequence of a protease produced by said tumor cell.

16. A method of producing a recombinant Paramyxoviridae virus comprising, in order, the steps of:

1) transfecting a eukaryotic cell line stably expressing T7 RNA polymerase with an infectious Paramyxoviridae viral genomic cDNA under the control of a T7 promoter;

2) infecting the transfected cells of step (1) with a helper virus expressing a selectable trait, and Paramyxoviridae viral N, P and L proteins;

3) contacting the infected, transfected cells of step (2) with cells that permit Paramyxoviridae virus infection and replication, under conditions permitting said infection and replication;

4) selecting syncytia formed on said cells that permit Paramyxoviridae virus infection and replication;

5) screening for and isolating said Paramyxoviridae lacking helper viral genetic material based upon the presence or absence of said selectable trait of said helper virus; and

6) expanding said Paramyxoviridae virus lacking helper viral genetic material to produce said recombinant Paramyxoviridae virus.

17. The method of claim 16 wherein said selectable trait is deletion of F protein.

18. The method of claim 16 wherein said selectable trait is expression an F protein that is cleavable by a protease other than furin.

19. The method of claim 16 wherein said selectable trait is expression of GFP.

20. A kit for treatment of a patient having a tumor, the kit comprising a replication-competent Paramyxoviridae virus comprising one or more of:

a) a nucleic acid sequence encoding a heterologous polypeptide, wherein upon said administration said heterologous polypeptide is detectable in a biological fluid of said patient, and detection of said heterologous polypeptide is indicative of Paramyxoviridae virus growth in said patient and reduction in tumor size;

b) a recombinant F protein, H protein, or M protein of said Paramyxoviridae virus that increases fusogenicity of said virus with said cells;

- c) a nucleic acid sequence encoding a cytokine; and
d) a Paramyxoviridae virus that is specific for cells of said tumor.

21. A method of treating a patient having a tumor in order to reduce tumor size, comprising administering to said patient a replication-competent Paramyxoviridae virus comprising two or more of a) a nucleic acid sequence encoding a heterologous polypeptide, wherein upon said administration said heterologous polypeptide is detectable in a biological fluid of said patient, and detection of said heterologous polypeptide is indicative of Paramyxoviridae virus growth in said patient and reduction in tumor size; b) a recombinant F protein, H protein, or M protein of said Paramyxoviridae virus that increases fusogenicity of said virus with said cells; c) a nucleic acid sequence encoding a cytokine; and d) a Paramyxoviridae virus that is specific for cells of said tumor.

22. The method of any one of claims 1, 5, 6, 7, 9, 16, 20 or 21 wherein said Paramyxoviridae virus is selected from the group consisting of Paramyxovirus, Morbillivirus, Rubulavirus and Pneumovirus.

23. The method of claim 22 wherein said Paramyxovirus is one of mumps virus, parainfluenza viruses type I or III, and Sendai virus.

24. The method of claim 22 wherein said Morbillivirus is one of measles virus, rinderpest virus, phocine distemper virus, and canine distemper virus.

25. The method of claim 22 wherein said Pneumovirus is one of human respiratory syncytial virus and bovine respiratory syncytial virus.

26. The method of claim 22 wherein said Rubulavirus is one of Simian virus type V or Newcastle disease virus.

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